

## ABSTRACT

The present invention relates PI3K crystals, polypeptide muteins, polypeptide fragments, antibodies thereto, nucleic acids coding for these polypeptides, methods of  
5 modifying PI3K $\gamma$  activity, and methods of modulating PI3K $\gamma$  activity. These include polypeptides and methods thereof, relating to, e.g., phospholipid binding, lipid kinase activity, modulating Ras activity in activating the PI3K $\gamma$ , binding of PI3K $\gamma$  to cell membranes, and modulating protein-protein interactions with PI3K $\gamma$ .